

### **REMARKS**

Prior to this amendment, claims 39-47 were pending. By this amendment, claims 40 and 45 have been cancelled, claim 48 has been added, and claims 39, 44, 46 and 47. Accordingly, claims 39, 41-44, and 46-48 are currently pending.

#### **Rejection under 35 U.S.C. §112, Second Paragraph**

In the Office Action, claims 39-47 were rejected under 35 U.S.C. §112, second paragraph allegedly for indefiniteness for the various reasons discussed below.

According to the examiner, claim 39, 44, 45 and 47 are vague and indefinite for reciting the phrase “in accordance with.” The examiner suggested substituting with the phrase “set forth in.” Applicants have complied with the examiner’s recommendation, and have amended claim 39, 44, 45 and 47. Thus, the rejection for reciting the phrase “in accordance with” is now moot and should be withdrawn.

Further, the examiner contends that claims 39, 44 and 47 are vague and indefinite for reciting the terms “homologous” or “functionally homologous protein thereof.” Applicants respectfully disagree.

The specification provides a clear definition of the term “homologous.” For example, in the paragraph bridging pages 4 and 5, it is disclosed that proteins with an E-value (Expect value) of more than  $10^{-10}$ , as determined by Blast or Blastp computer programs, are not considered to be homologous. Therefore, the term “homologous” is clear and not vague and indefinite.

With regard to the terms “functionally homologous protein,” applicants have amended the claims to remove this phrase. Accordingly, the rejection of the claims for reciting the terms “functionally homologous protein” is now moot and should be withdrawn.

Moreover, the examiner alleges that claim 39 is vague and indefinite for failing to state that the protein is “isolated” and/or “purified.” Applicants have amended claim 39 by inserting the word “isolated.” Accordingly, claim 39 now includes that the protein is isolated.

Claim 39 was further rejected for being vague and indefinite for the phrase “wherein the composition raises an immune response to streptococcal infections.” According to the examiner, it is not clear how a protein can raise an immune response to an infection. Applicants have amended claim 39 to state that the protein raises an immune response to *Streptococcus pneumoniae*.

The examiner states that claim 44 was rejected for containing a grammatical error, e.g., “method for preparing of an immunogenic composition.” The examiner recommended deleting the word “of.” Applicants have complied with the examiner’s recommendation.

Additionally, the examiner states that the term “or a recombinant or synthetic protein thereof” in part (a) of claim 44 is vague and indefinite. The examiner states that the claim should actively state that the recombinant or synthetic proteins have SEQ. ID. NO: 2. Alternatively, the examiner states that the phrase should be deleted since the broad statement “isolating a protease maturation protein of *S. pneumoniae*, wherein the protein has an amino acid sequence as set forth in SEQ. ID NO: 2” would encompass isolating the protein in any way, i.e., naturally, recombinantly, synthetically.

Applicants agree with the examiner that the broad statement “isolating a protease maturation protein...” in part (a) of claim 44 does not limit the way the protein is isolated and, therefore does not affect the scope of the claims. Accordingly, as suggested by the examiner, applicants have deleted the phrase “or a recombinant or synthetic protein thereof” from the claim.

Claim 45 was rejected for providing for the use of a protease maturation protein without setting forth any steps. Applicants have cancelled claim 45. Therefore, the rejection of claim 45 is now moot.

As requested by the examiner, applicants have corrected the typographical error in claim 46, by replacing the word “raining” with “raising.”

Applicants very much appreciate the examiner’s numerous helpful suggestions.

Accordingly, in view of the above, applicants respectfully request that the rejection of claims 39-47 under 35 U.S.C. §112, second paragraph be reconsidered and withdrawn.

**Rejection under 35 U.S.C. §112, First Paragraph**

Claims 39-47 were rejected under 35 U.S.C. §112, first paragraph. The examiner concedes that the specification is enabled for “an immunogenic composition comprising an isolated protease maturation proteins of *S. pneumoniae*, wherein the protein has an amino acid sequence as set forth in SEQ. ID. NO:2 and methods of raising an immune response against *S. pneumoniae* through the administration of said compound. However, the examiner alleges that the specification does not reasonably provide enablement for homologous or functionally homologous proteins of SEQ. ID. NO:2, or methods for raising an immune response using the homologous or functionally homologous proteins of SEQ. ID. NO:2.

Applicants respectfully disagree with the examiner’s contention that homologous proteins of SEQ. ID NO:2 are not enabled.

The specification, in fact, provides guidance to the skilled artisan for determining whether an amino acid sequence is homologous to SEQ. ID NO:2. For example, in the paragraph bridging pages 4 and 5 of the application, it is explained that proteins which have an

Expect value, as determined by Blast or Blastp computer programs, of more than  $10^{-10}$  are not considered to be homologous.

An Expect value having a cut-off of  $10^{-10}$  is a very stringent criteria for determining whether two amino acid sequences are homologous. The Expect value and the computer programs used to determine it, are standard tools routinely used by those in the art.

Furthermore, the Pmp protein (protein of SEQ. ID. NO:2) is a highly conserved protein over the different strains of *S. pneumoniae*. See page 6, lines 30-31 of the specification. Therefore, a skilled artisan, using routine techniques, can determine which amino acids are conserved. It is further well known to those skill in the art that conserved amino acids appear to be crucial for the structure and/or function of the protein. Thus, a person skilled in the art would know to substitute or delete non-conserved amino acids.

Thus, using standard techniques in the art and guidance in the specification, one can easily determine whether a protein is considered to be homologous to SEQ. ID. NO:2. It is logical and expected that such highly homologous proteins (e.g., those having an Expect value in accordance with the specification) to SEQ. ID. NO: 2 would also raise an immune response to *S. pneumoniae*.

For the above reasons, applicants respectfully request that the rejection of the claims under 35 U.S.C. §112 allegedly for lack of enablement be reconsidered and withdrawn.

**Rejection under 35 U.S.C. §102(b) over Kunsch et al. (WO 98/18930) and Rejection under 35 U.S.C. §102(e) over Black et al. (U.S. Patent No. 6,348,328 B1)**

Claims 39-47 were rejected under 35 U.S.C. §102(b) for allegedly being anticipated by Kunsch et al. (WO 98/18931). The examiner states that a polypeptide disclosed in Table 1 of Kunsch et al. has 213 identical amino acids to the claimed SEQ. ID NO:2, which is 322 amino

acids in length. Therefore, the examiner concludes that the instant claims encompass the polypeptide disclosed in Kunsch et al.

Claims 39-47 were also rejected under 35 U.S.C. §102(e) for allegedly being anticipated by Black et al. (U.S. Patent No. 6,348,328 B1). According to the examiner, Black et al. teach a polypeptide which has 48 identical amino acids to the claimed SEQ. ID. NO:2. The examiner states that the instant claims include "homologous" polypeptides. Therefore, the examiner concludes that the polypeptide disclosed in Black et al. is encompassed in the instant claims.

Applicants respectfully disagree. Using the number of identical amino acids the examiner provided, the polypeptide disclosed in Kunsch et al. results in about a 66% match to SEQ. ID. NO:2. The polypeptide of Black et al. results in about a 13% match to SEQ. ID. NO:2.

As stated above, for a polypeptide to be considered homologous to SEQ. ID. NO:2, the Expect value of the polypeptide must **not** be more than  $10^{-10}$ .

The computer program used for the sequence comparison is not able to calculate an Expect value for comparisons with non-equal sequence lengths. However, it is readily apparent to a person skilled in the art that such a low percentage match will not yield an Expect value of not more than  $10^{-10}$ . See the Rule 132 Declaration executed by Dr. Hermans. Applicants will forward to the examiner exhibit 1 of the Rule 132 Declaration once it is received.

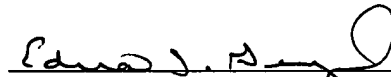
In paragraph 15 of the Rule 132 Declaration of Dr. Hermans states that it would be apparent to one skilled in the art that, even if the proteins being compared were of equal lengths, such a low percentage match (e.g., 57.7% match for the Kunsch et al. polypeptide and 20.3% match for the Black et al peptide to SEQ. ID. NO:2) would not yield an Expect value that is equal to or less than  $10^{-10}$ , as is required in the claimed invention.

Therefore, the polypeptides of Kunsch et al. and Black et al. are not considered homologous of SEQ. ID. NO:2, as is required in the claimed invention.

For the above reasons, applicants respectfully request that the rejection of the claims under 35 U.S.C. §102(b) over Kunsch et al. and under 35 U.S.C. §102(e) over Black et al. be reconsidered and withdrawn.

Allowance of the pending claims is earnestly requested. If the examiner has any questions regarding this amendment, she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

  
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